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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,323	07/09/2003	Laurence A. Cole	MBHB 03-411-A	1369

7590 03/24/2010

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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
03/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/616,323	COLE, LAURENCE A.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 2, 5-16, 46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *12-16 and 47* is/are allowed.

6)☒ Claim(s) *1,5-11 and 46* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed January 12, 2010 in response to the Office Action of October 5, 2010 is acknowledged and has been entered. Claims 1 and 12 have been amended and new claims 55-61 have been added. Claims 1, 2, 5-16, 46 and 47 are currently being examined.

Oath/Declaration

2. The Declaration of Dr. Laurence A. Cole under 37 CFR 1.132 filed 01/12/2010 is sufficient to overcome the rejection of claim 1, 2, 5-16, 46 and 47 under 35 U.S.C. 112, first paragraph.

3. The Declaration of Dr. Laurence A. Cole under 37 CFR 1.132 filed 1/12/2010 is sufficient to overcome the rejection of claims 1, 2, 5-16, and 47 under 35 U.S.C. 102(a) as based upon Khanlian et al. (American J. of Obstetrics and Gynecology May 2003 188:1254-9).

Priority

4. The priority date of 7/9/2003 for claims 1, 2, 5-16, 46 and 47 is maintained for the reasons set forth in section 2 of the Office Action of October 5, 2010. Applicants argue that Office Action of October 5, 2010 provides support for the instant invention, but does not specifically point to the support. Thus, for the reasons previously set for the priority date is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1, 5-11, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over USPN 6,927,034 (O'Conner et al. May 13, 1999) in view of Cole et al. (Clinical Chemistry 1999: 45: 2109-2119, IDS) and in further view of Cole et al. (Clinical Chemistry 2001, 47:308-315, IDS).

USPN 6,927,034 teaches obtaining a urine sample from a patient who is pregnant (which would be a patient at risk for gestational trophoblastic disease) and measuring the total amount of any intact hCG in the sample and measuring the amount of hyperglycosylated hCG/ITA (EPMI) with the B152 antibody. USPN 6,927,034 teaches comparing the ratio of ITA (EPMI) to intact hCG. USPN 6,927,034 teaches determining the presence of hydatidiform mole or choriocarcinoma when the ratio of ITA (EPMI) to hCG is greater than 1.0, which would be an amount of hCG that is ITA of greater than 50%, e.g. a ratio greater than 1 part ITA to 1 part intact hCG would be greater 50% (1 part ITA÷ (1 part ITA + 1 part intact hCG)). See claims 1-10 and Example 4.

USPN 6,927,034 does not teach determining that invasive trophoblast cells are present in the patient or taking the sample from patients previously diagnosed as having gestational trophoblastic disease.

Cole et al. (1999) teach that hyperglycosylated hCG (ITA) detected with the B152 accounted for virtually all hCG in five choriocarcinoma patients. Cole et al. (1999) teach that hyperglycosylated hCG is produced by invasive or cancerous trophoblast cells in choriocarcinoma. See p. 2110-1st col.

Cole et al. (2001) teach that trophoblastic disease in women includes choriocarcinoma, hydatidiform mole, and placental site trophoblastic disease. Cole et al. (2001) teach that these diseases are major sources of hCG and hyperglycosylated hCG. See p. 309.

It would have been *prima facie* obvious at the time the invention was made to determine that invasive trophoblast cells were present in patients determined to have choriocarcinoma or hydatidiform mole by the method of USPN 6,927,034, where an amount of hCG that is ITA is greater than 50% (which is greater than 30%), because Cole et al. (1999) teach that hyperglycosylated hCG is produced by invasive or cancerous trophoblast cells in choriocarcinoma. Thus, one of skill in the art would have been motivated to make such a determination given that it was known that invasive or cancerous trophoblast cells are the source of ITA in patients with trophoblastic disease. Additionally, it would have been obvious to take the samples from women who were previously diagnosed with various forms of trophoblastic disease with the method of to USPN 6,927,034 make a determination of the presence of invasive trophoblast cells based ITA and hCG levels to monitor these patient for recurrence of the disease. One of skill in the art would have had a reasonable expectation of success given that

determination of hCG and ITA levels and there production by invasive trophoblast cells was known in the art and USPN 6,927,034 taught how to use the measurement of these levels for the detection of gestational trophoblastic malignancy.

6. All other objections and rejections recited in Office Action of October 5, 2010 are withdrawn.

7. Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Claims 12-16 and 47 appear allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/
Primary Examiner, Art Unit 1642